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(54) Title: 3'-PRODRUGS OF 2'-DEOXY- β -L-NUCLEOSIDES

(57) Abstract: The present invention relates to compounds, compositions and methods for the treatment of a host infected with a hepatitis B virus. Specifically, compounds and compositions of 3'-esters of 2'-deoxy- β -L-nucleosides are disclosed, which can be administered either alone or in combination with other anti-hepatitis B agents. Compounds and compositions of 3',5'-esters of 2'-deoxy- β -L-nucleosides are disclosed, which can be administered either alone or in combination with other anti-hepatitis B agents, are also disclosed.

INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07H19/06 C07H19/16 A61K31/7068 A61P31/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 09531 A (NOVIRIO PHARMACEUTICALS LIMITE;IMBACH JEAN LOUIS ; GOSSELIN GILLES) 24 February 2000 (2000-02-24) cited in the application the whole document	1-194
X	V. SKARIC ET AL.: "Aminoacyl derivatives of 4-thiothymidine, cytosine and cytidine" CROATICA CHEMICA ACTA, vol. 48, no. 3, 1976, pages 351-359, XP001034973 page 352 --- -/--	1-4,6-8

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WANG P ET AL: "RECENT ADVANCES IN L-NUCLEOSIDES: CHEMISTRY AND BIOLOGY" ANTIVIRAL RESEARCH, ELSEVIER SCIENCE BV., AMSTERDAM, NL, vol. 46, no. 1/2, 1998, pages 19-44, XP000944025 ISSN: 0166-3542 scheme 2 conclusions ---	1,156
X	US 5 559 101 A (WEIS ALEXANDER L ET AL) 24 September 1996 (1996-09-24) the whole document ---	1,2
X	WO 92 08727 A (CONSIGLIO NAZIONALE RICERCHE ;MENARINI RICERCHE SUD SPA (IT)) 29 May 1992 (1992-05-29) the whole document ---	1,2
X	BOUDOU V ET AL: "A new and convenient approach for the synthesis of ribo- and 2'-deoxyribo-beta-L-furanonucleosides starting from beta-L-xylofuranonucleosides" NUCLEOSIDES & NUCLEOTIDES, MARCEL DEKKER, INC, US, vol. 18, no. 45, 1999, pages 607-609, XP002164642 ISSN: 0732-8311 the whole document ---	1,156
A	RYU E K ET AL: "AMINOACYL DERIVATIVES OF NUCLEOSIDES, NUCLEOTIDES, AND POLYNUCLEOTIDES. XXVII GENERAL SYNTHESIS OF 2'(3')-O-AMINOACYL DINUCLEOSIDE PHOSPHATES DERIVED FROM THE AA-TRNA TERMINUS" JOURNAL OF CARBOHYDRATES. NUCLEOSIDES NUCLEOTIDES, MARCEL DEKKER, BASEL, CH, vol. 4, no. 6, 1977, pages 387-408, XP000564974 ISSN: 0094-0585 structures 4b-e -----	4

INTERNATIONAL SEARCH REPORT

information on patent family members

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Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0009531	A	24-02-2000	AU	5475799 A		06-03-2000
			CN	1320128 T		31-10-2001
			EP	1104436 A2		06-06-2001
			WO	0009531 A2		24-02-2000
<hr/>						
US 5559101	A	24-09-1996	EP	0788506 A2		13-08-1997
			JP	10507772 T		28-07-1998
			WO	9613512 A2		09-05-1996
<hr/>						
WO 9208727	A	29-05-1992	IT	1246983 B		12-12-1994
			AU	8923291 A		11-06-1992
			WO	9208727 A1		29-05-1992
<hr/>						